AMENDMENT

In the Specification:

Please amend the paragraph beginning at page 1, line 23 as follows:

Virulence-associated antigens involved in adhesion have been identified in several bacteria and other organisms, and these antigens are useful for the diagnosis, prevention and treatment of bacterial infections (particularly those caused by virulent strains). In particular, antigens have been identified in: *Haemophilus influenzae* biogroup *aegyptius* (SEQ ID NO: 1); *Escherichia coli* K1 (SEQ ID ~~NO~~[S] ~~: 2 & 3~~ NOS: 2 and 3) and also in EHEC strain EDL933; *Actinobacillus actinomycetemcomitans* (SEQ ID NO:4); *Haemophilus somnus* (SEQ ID NO: 5); *Haemophilus ducreyi* (SEQ ID NO:6); EPEC *E. coli* strain E2348/69 (SEQ ID NO:7); EPEC(SEQ ID NO: 18); EAEC *E.coli* strain 042 (SEQ ID ~~NO~~[S] ~~: 8 & 9~~ NOS: 8 and 9); uropathogenic *E.coli* (SEQ ID NO: 10); *Shigella flexneri* (SEQ ID NO: 11); *Brucella melitensis* (SEQ ID NO: 12); *Brucella suis* (SEQ ID NO: 13); *Ralstonia solanacearum* (SEQ ID NO: 14); *Sinorhizobium meliloti* (SEQ ID NO: 15); *Bradorhizobium japonicum* (SEQ ID NO: 16); and *Burkholderia fungorum* (SEQ ID NO:17).

Please amend the paragraph at page 2, line 10 as follows:

The positions of these features in SEQ ID ~~NO~~[S] NOS: 1 to 18 are as follows:

Please amend the paragraph beginning at page 2, line 13 as follows:

The invention provides a polypeptide comprising one or more of the following amino acid sequences: any of SEQ ID ~~NO~~[S] NOS: 1 to 18, SEQ ID NO: 51, and SEQ ID NO: 54.

Please amend the paragraph beginning at page 2, line 15 as follows:

The invention also provides a polypeptide comprising an amino acid sequence: (a) having at least *m*% identity to one or more of SEQ ID ~~NO~~[S] NOS: 1-18, 51 ~~&~~ and 54, where *m* is 50 or more (*e.g.* 60, 65, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 99.5 or more), and/or (b) which is a fragment of at least *n* consecutive amino acids of one or more of SEQ ID ~~NO~~[S] NOS: 1-18, 51 ~~&~~ and 54, wherein *n* is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These polypeptides include variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants, *etc.*) of SEQ ID ~~NO~~[S] NOS: 1-18, 51 ~~&~~ and 54.

Please amend the paragraph beginning at page 3, line 4 as follows:

Preferred fragments of (b) comprise an epitope from one or more of SEQ ID ~~NO~~[S] NOS: 1-18, 51 ~~&~~ and 54, preferably a B-cell epitope. B-cell epitopes can be identified empirically or can be predicted algorithmically.

Please amend the paragraph beginning at page 3, line 7 as follows:

Other preferred fragments of (b) lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 45 or more) from the N-terminus of the relevant amino acid sequence from SEQ ID ~~NO~~[S] NOS: 1-18, 51 ~~&~~ and 54. In particular, preferred fragments omit at least the N-terminus leader sequence (and the omitted leader sequence may be replaced by a heterologous leader sequence).

Please amend the paragraph beginning at page 3, line 12 as follows:

Other preferred fragments omit one or more (*i.e.* 1, 2, or 3) of the four domains of SEQ ID ~~NO~~[S] NOS: 1-18 ~~&~~ and 51, based on the above table. Other preferred fragments consist of one or more (*i.e.* 1, 2, or 3) of the four domains of SEQ ID ~~NO~~[S] NOS: 1-18 ~~&~~ and 51.

Please amend the paragraph beginning at page 3, line 17 as follows:

The invention also provides polypeptides of the formula **NH2-A-{-X-L-}$_x$-B- COOH**, wherein:

- X comprises an amino acid sequence: (a) having at least *m*% identity to one or more of SEQ ID ~~NO~~^{S} NOS: 1-18, 51 ~~&~~ and 54; and/or (b) which is a fragment of at least *n* consecutive amino acids of one or more of SEQ ID ~~NO~~^{S} NOS: 1-18, 51 ~~&~~ and 54,as defined above;
- L is an optional linker amino acid sequence;
- A is an optional N-terminal amino acid sequence;
- B is an optional C-terminal amino acid sequence; and
- *x* is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18 (preferably *x*=2).

Please amend the paragraph beginning at page 4, line 23 as follows:

wherein:

- A is an optional sequence as defined above (preferably at the N-terminus of the polypeptide);
- B is an optional sequence as defined above (preferably at the C-terminus of the polypeptide);
- W_1 is an optional amino acid sequence: (a) having at least *m*% identity to the leader peptide of one or more of SEQ ID ~~NO~~^{S} NOS: 1-18 ~~&~~ and 51; and/or (b) which is a fragment of at least *n* consecutive amino acids of the leader peptide of one or more of SEQ ID ~~NO~~^{S} NOS: 1-18 ~~&~~ and 51;
- W_2 is an optional amino acid sequence: (a) having at least *m*% identity to the globular head domain of one or more of SEQ ID ~~NO~~^{S} NOS: 1-18 ~~&~~ and 51; and/or (b) which is a fragment of at least *n* consecutive amino acids of the globular head domain of one or more of SEQ ID ~~NO~~^{S} NOS: 1-18 ~~&~~ and 51;
- W_3 is an optional amino acid sequence: (a) having at least *m*% identity to the coiled-coil domain of one or more of SEQ ID ~~NO~~^{S} NOS: 1-18 ~~&~~ and 51; and/or

(b) which is a fragment of at least *n* consecutive amino acids of the coiled-coil domain of one or more of SEQ ID ~~NO~~[S] NOS: 1-18 ~~&~~ and 51;

- W_4 is an optional amino acid sequence: (a) having at least *m*% identity to the transmembrane anchor region of one or more of SEQ ID ~~NO~~[S] NOS: 1-18 ~~&~~ and 51; and/or (b) which is a fragment of at least *n* consecutive amino acids of the kansmembrane anchor region of one or more of SEQ ID ~~NO~~[S] NOS: 1-18 ~~&~~ and 51;

provided that at least one of W_1, W_2, W_3 or W_4 is present.

Please amend the paragraph beginning at page 9, line 33 as follows:

Vaccines of the invention may be administered in conjunction with other immunoregulatory agents. In particular, compositions will usually include an adjuvant. Preferred further adjuvants include, but are not limited to: (A) aluminium salts, including hydroxides (*e.g.* oxyhydroxides), phosphates (*e.g.* hydroxyphoshpates, orthophosphates), sulphates, *etc.* {*e.g.* see chapters 8 & 9 of ref. 23}), or mixtures of different aluminium compounds, with the compounds taking any suitable form (*e.g.* gel, crystalline, amorphous, *etc.*), and with adsorption being preferred; (B) MF59 (5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a microfluidizer) {see Chapter 10 of 23; see also ref. 24}; (C) liposomes {see Chapters 13 and 14 of ref. 23}; (D) ISCOMs {see Chapter 23 of ref. 23}, which may be devoid of additional detergent {25}; (E) SAF, containing 10% Squalane, 0.4% Tween 80, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion {see Chapter 12 of ref. 23}; (F) ~~Ribi~~[TM] RIBI[TM] adjuvant system (RAS), (Ribi Immunochem) containing 2% Squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphorylipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (~~Detox~~[TM] DETOX[TM]); (G) saponin adjuvants, such as QuilA or QS21 {see Chapter 22 of ref. 23}, also known as ~~Stimulon~~[TM]

STIMULON™ {26}; (H) chitosan {*e.g.* 27}; (I) complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA); (J) cytokines, such as interleukins (*e.g.* IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12, *etc.*), interferons (*e.g.* interferon-γ), macrophage colony stimulating factor, tumor necrosis factor, *etc.* {see Chapters 27 & 28 of ref. 23}; (K) monophosphoryl lipid A (MPL) or 3-O-deacylated MPL (3dMPL) {*e.g.* chapter 21 of ref. 23}; (L) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions {28}; (M) a polyoxyethylene ether or a polyoxyethylene ester {29}; (N) a polyoxyethylene sorbitan ester surfactant in combination with an octoxynol {30} or a polyoxyethylene alkyl ether or ester surfactant in combination with at least one additional non-ionic surfactant such as an octoxynol {31}; (N) a particle of metal salt {32}; (O) a saponin and an oil-in-water emulsion {33}; (P) a saponin (*e.g.* QS21) + 3dMPL + IL-12 (optionally + a sterol) {34}; (Q) *E. coli* heat-labile enterotoxin ("LT"), or detoxified mutants thereof, such as the K63 or R72 mutants {*e.g.* Chapter 5 of ref. 35}; (R) cholera toxin ("CT"), or detoxified mutants thereof {*e.g.* Chapter 5 of ref. 35}; (S) double-stranded RNA; (T) microparticles (*i.e.* a particle of ~100nm to ~150μm in diameter, more preferably ~200nm to ~30μm in diameter, and most preferably ~500nm to ~10μm in diameter) formed from materials that are biodegradable and non-toxic (*e.g.* a poly(a-hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone, *etc.*), with poly(lactide-co-glycolide) being preferred, optionally treated to have a negatively-charged surface (*e.g.* with SDS) or a positively-charged surface (*e.g.* with a cationic detergent, such as CTAB) ; (U) oligonucleotides comprising CpG motifs *i.e.* containing at least one CG dinucleotide, with 5-methylcytosine optionally being used in place of cytosine; (V) monophosphoryl lipid A mimics, such as aminoalkyl glucosaminide phosphate derivatives *e.g.* RC-529 {36}; (W) polyphosphazene (PCPP); (X) a bioadhesive {37} such as esterified hyaluronic acid microspheres {38} or a mucoadhesive selected from the group consisting of cross-linked derivatives of poly(acrylic acid), polyvinyl alcohol, polyvinyl pyrollidone, polysaccharides and carboxymethylcellulose; or (Y) other substances that act as immunostimulating agents to

enhance the effectiveness of the composition {*e.g.* see Chapter 7 of ref. 23}. Aluminium salts and MF59 are preferred adjuvants for parenteral immunisation. Mutant toxins are preferred mucosal adjuvants.

Please amend the paragraph beginning at page 16, line 24 as follows:

Figure 30 shows immunofluorescence microscopy analysis of ~~with~~ E. coli-pET HadA na and Chang epithelial cells. Extracellular bacteria are seen ~~in green~~ as white; intracellular bacteria are ~~red~~ grey.

Please amend the paragraph beginning at page 28, line 14 as follows:

Adhesion and invasion were confirmed by immunofluorescence microscopy analysis (Figure 30). Extracellular bacteria (~~green~~ white) and intracellular bacteria (~~red~~ grey) can be seen.